EXHIBIT K

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
AT CHARLESTON

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION **THIS DOCUMENT RELATES TO WAVE 1**	**Master File No. 2:12-MD-02327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**

RULE 26 EXPERT REPORT OF HOWARD JORDI, PhD

I, Dr. Howard Jordi have been asked to provide my expert opinion concerning the potential for Prolene polypropylene to undergo *in vivo* degradation. My opinions contained within this report relate to all of Ethicon's Prolene polypropylene mesh devices marketed for the treatment of pelvic organ prolapse and stress urinary incontinence, including Ethicon's Prolift, Prosima and TVT devices. I offer all opinions contained herein to a reasonable degree of scientific certainty or probability based on my extensive knowledge, training, education and experience, my thorough review of the relevant scientific publications concerning polypropylene degradation, my thorough review of Ethicon's internal documents and my analysis of data collected by me or at my direction using reliable scientific techniques recognized in the field of polymer science as reliable methods for the assessment of degradation of polymers generally and polypropylene specifically. I also rely on my prior Rule 26 Expert Reports served in the Lewis v. Ethicon and Bellew v. Ethicon matters.[1]

I. Background and Qualifications

I received my undergraduate degree in Chemistry from Northern Illinois University in 1967 and my Ph.D. in biochemistry from the same university in 1974.

From 1973-1977, I served in the United States Army Institute of Dental Research where I characterized various drugs contained in biodegradable copolymers of polylactic and polyglycolic acid. I then worked at Water's Associates from 1977-1980. Water's is a world leader in the sale of a wide range of analytical technologies including liquid chromatography, mass spectrometry, rheometry and microcalorimetry. At Waters, I progressed from a Biological Applications chemist to the laboratory manager for the life science division and finally to the Chemicals Applications Manager for the Chromatography Supplies Division.

[1] Lewis v. Ethicon, et al. Rule 26 Expert Report attached as Exhibit A; Bellew v. Ethicon, et al. Rule 26 Expert Report attached as Exhibit B.

I am the founder of Jordi Labs and served as president and CEO from 1980-2008. Jordi Labs was founded to provide high quality analytical services to the polymer and plastics industries. In my role as President and CEO, I developed hundreds of analytical methods and have analyzed all of the major polymer systems (polypropylene, polyethylene, urethanes, styrenics, etc.). In this capacity, I have been analyzing polypropylenes for over 25 years. I have deformulated numerous polypropylene samples including identifying and quantifying their additive packages and have been aiding clients for over 25 years in the identification of the root cause of failure in polypropylene systems. I have served extensively as a consultant on polymer related failures for a wide range of industrial clients and have over 40 years of practical experience in the analytical chemistry of polymers. I have in-depth knowledge of a wide range of analytical techniques including FTIR, NMR, DSC, TGA, HPLC, SEM, GPC, DMS, LCMS, GCMS, nanothermal analysis, H-GCMS and PYMS among others. Jordi Labs currently offers over 20 different analytical techniques. I have developed a range of polymeric chromatography columns for polymer molecular weight determination, some of which are patented.

(Attached as Exhibit "C" to this report is a true and accurate copy of my current curriculum vitae. A list of my Reliance Materials is attached as Exhibit "D")

II. Degradation

Degradation Pathways of Polypropylene

Most polymers undergo degradation when exposed to appropriate conditions. Polymer degradation may refer to change in the polymeric properties such as structural integrity, color, shape or tensile strength, to name a few. The degradation process involves several physical and/or chemical processes which are accompanied by structural changes in the polymer leading to significant deterioration of the quality of the polymer.[2,3,4] There are several different types of degradation mechanisms:

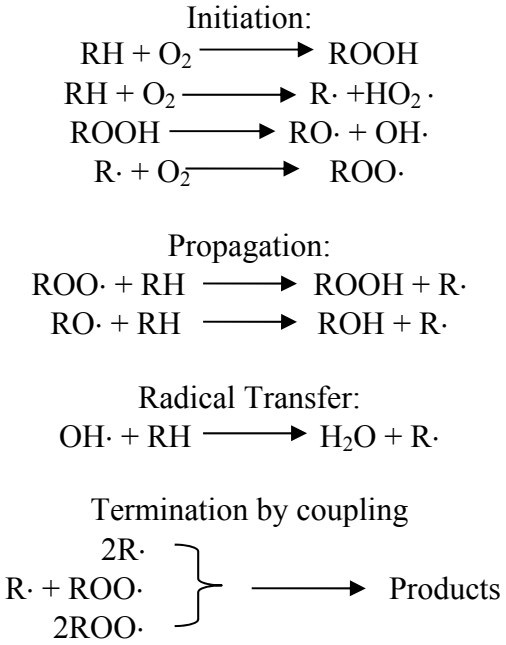
1. Photochemical degradation: Exposure to UV and/or visible light
2. High-energy radiation induced degradation: Exposure to X-rays, γ-rays, etc.
3. Mechanical degradation: Stress forces, abrasive forces during processing or application
4. Thermal degradation: Exposure to heat
5. Chemical degradation: Hydrolysis or exposure to acids, alkalis, salts, reactive gases, etc.
6. Oxidation: Reaction with oxygen, ozone, peroxides, etc.
7. Biodegradation: Interaction with enzymes and microbes
8. Combination of two or more of the above mechanisms

The physiological environment in the human body does not involve many of these conditions such as exposure to light. In the context of non-hydrolyzable hydrophobic polymers (here

[2] Cornelia Vasile, Degradation and decomposition, in Handbook of Polyolefin, eds. Cornelia Vasile and Raymond B. Seymour (Marcel Dekker Inc, New York, USA) 1993, 479-552.
[3] A. Ravve, Degradation of Polymers, in Principles of Polymer Chemistry 2nd Ed., (Kluwer Academic/Plenum Publishers, New York, USA) 2000. 581-616.
[4] Devesh Tripathi, Practical Guide to Polypropylene, (Rapra Technology Ltd. Shropshire, UK) 2002.

isotactic polypropylene) used as medical devices oxidation, biodegradation and mechanical degradation pathways are the most pertinent and will be discussed in detail below.

Oxidative degradation: Polypropylene is highly susceptible to attack by oxidants such as atmospheric oxygen, ozone or peroxides.[5,6,7,8] Oxidative degradation can alter its molecular weight and polydispersity index (PDI) through cleavage of the long polypropylene chains into smaller fragments. The process of oxidative degradation of polypropylene and the steps involved are described in Scheme 1.[9,10]



Scheme 1. Mechanism of Oxidative Degradation of Polypropylene (RH = polypropylene)

As a result, polypropylene is an incompatible material under oxidative conditions.[11,12] While oxidants such as ozone are not present in a biological system, the presence of oxygen (O_2) and its

[5] Cornelia Vasile, Degradation and decomposition, in Handbook of Polyolefin, eds. Cornelia Vasile and Raymond B. Seymour (Marcel Dekker Inc, New York, USA) 1993, 479-552

[6] A. Ravve, Degradation of Polymers, in Principles of Polymer Chemistry 2nd Ed., (Kluwer Academic/Plenum Publishers, New York, USA) 2000. 581-616.

[7] Denis Bertin, Marie Leblanc, Sylvain R. A. Marque and Didier Siri, Polymer Degradation and Stability 95 (2010) 782-791.

[8] R. A. Silva, P. A. Silva and M. E. Carvalho, Materials Science Forum 539-543 (2007) 573-576.

[9] Cornelia Vasile, Degradation and decomposition, in Handbook of Polyolefin, eds. Cornelia Vasile and Raymond B. Seymour (Marcel Dekker Inc, New York, USA) 1993, 479-552.

[10] Timothy C Liebert, Richard P. Chartoff, Stanley L. Cosgrove and Roberts S. McCuskey Journal of Biomedical Materials Research 10 (1976) 939-951.

[11] R. A. Silva, P. A. Silva and M. E. Carvalho, Materials Science Forum 539-543 (2007) 573-576.

[12] Kurt Schwarzenbach, Antioxidants, in Plastics Additives 2nd Ed., R. Gachter and H. Muller (Hanser Publishers, Munich Germany) 1987, 18.

other forms such as superoxides, peroxides and free radicals makes the human body a powerful oxidizing environment to polymers and oxidation occurs via similar processes.[13]

Biodegradation: There is ample evidence in the literature that indicates that polypropylene undergoes degradation in the biological system.[14,15,16,17] The physiological environment of the polymer can critically control its function and performance.

Upon implantation of polypropylene in the body, white blood cells begin to produce oxidants such as hydrogen peroxide and hypochlorous acid that continue the oxidation induced during sterilization or manufacturing. Oxidation of polypropylene produces more free radicals which causes depolymerization, oxidative degradation, hydrolysis and stress cracking. Enzymes present in the body are able to catalyze these reactions at body temperature. Breakdown of the polymeric chains can then cause the surface of a polymeric implant to crack.[18]

Macrophages in the body produce large amounts of both superoxide (O_2^-) and hydrogen peroxide (H_2O_2) when faced with infectious agents or other foreign materials.[19] This process known as the oxidative burst is the one electron reduction of oxygen (O_2) to O_2^- and is catalyzed by NADPH oxidase or NADH oxidase utilizing NADPH or NADH as substrates.

$$2O_2 + NADPH \longrightarrow 2O_2^- + NADP^+ + H^+$$

Superoxide radicals react to produce hydrogen peroxide with the reaction being catalyzed by superoxide dismutase (SOD).

$$2O_2^- + 2H^+ \xrightarrow{SOD} H_2O_2 + O_2$$

While both superoxide and hydrogen peroxide can react with polypropylene, the presence of metal ions such as Fe(II) and Cu(I) leads to the generation of hydroxyl radicals which are even more reactive towards polypropylene.

$$O_2^- + M^{n+} \longrightarrow O_2 + M^{(n-1)+}$$
$$H_2O_2 + M^{(n-1)+} \longrightarrow OH\cdot + OH^- + M^{n+}$$

Net Reaction:

$$O_2^- + H_2O_2 \longrightarrow O_2 + OH\cdot + OH^-$$

[13] Timothy C Liebert, Richard P. Chartoff, Stanley L. Cosgrove and Roberts S. McCuskey Journal of Biomedical Materials Research 10 (1976) 939-951.
[14] Timothy C Liebert, Richard P. Chartoff, Stanley L. Cosgrove and Roberts S. McCuskey Journal of Biomedical Materials Research 10 (1976) 939-951.
[15] Donald R. Ostegard, International Urogynecology Journal 22 (2011) 771-774.
[16] D. F. Williams, Journal of Materials Science 17 (1982) 1233-1246 and references therein.
[17] C. D. Klink, K. Junge, M. Binnebösel, H. P. Alizai, J. Otto, U. P. Neumann and U. Klinge, Journal of Investigative Surgery 24 (2011) 292-299.
[18] Gina Sternschuss, Donald R. Ostergard and Hiren Patel, The Journal of Urology 188 (2012) 27-32.
[19] S. A. M. Ali, S. -P. Zhong, P. J. Doherty and D. F. WIlliams, Biomaterials 14 (1993) 648-656.

The overall net reaction shown above is usually referred to as metal catalyzed Haber-Weiss reaction. Most of the hydroxyl radicals generated *in vivo* are formed from the metal ion dependent breakdown of hydrogen peroxide.

Mechanical degradation: Mechanical degradation or stress-induced cracking of polymers is a degradation pathway which involves irreversible breakdown (cracking, fracture, deformation etc.) of the polymeric material under mechanical stress.[20,21] Environmental stress cracking (ESC) is cracking of a polymer due to the combined action of a stress and a fluid. It is associated with the phenomenon of crazing and solvent plasticization of the polymer.[22] As mentioned earlier, the environment of a polymer can have a significant effect on the polymer. The polymer can absorb the fluid surrounding it and the polymer swells causing compressive stress at the surface. This initiates a phenomenon known as crazing which is the mechanical separation of the entangled chains of the polymer. Solvent induced crazes grow more quickly and to greater dimensions than those in inert environments. The crazes that are under the influence of stress act as initiation sites for cracks. Other factors influencing cracking in crazed polymers include time, temperature, molecular weight of the polymer, its structure and thermal history. The stressed chains become mechanically excited. Deexcitation of these chains occurs via various phenomena such as conformational changes, or bond scission/breakage causing the polymer to crack. The ultimate response is a fractured polymeric material. In the conclusion of a 2010 study where polypropylene explants from the human body were characterized, Clave et al. state that "The diffusion of organic molecules into the polymer (especially esterified fatty acids or cholesterol) may be a cause of the polymer structure degradation."[23] Molecules like fatty acids and cholesterol are hydrophobic and have similar chemistries and would be expected to be compatible with polypropylene chains. These molecules would easily diffuse into the amorphous regions of polypropylene polymers initiating the formation of crazing.

III. The Scientific Literature Demonstrates That Polypropylene Mesh Devices, Including Ethicon's Prolene TVT Device Will Undergo *In Vivo* Degradation

Scientific publications dating back at least 50 years confirm that polypropylene, including Prolene used in Ethicon's pelvic floor devices, degrades while in the human body.

Scientists have been studying polymer degradation, including polypropylene degradation, since at least the 1960s and have uniformly concluded that polypropylene is susceptible to degradation

[20] Cornelia Vasile, Degradation and decomposition, in Handbook of Polyolefin, eds. Cornelia Vasile and Raymond B. Seymour (Marcel Dekker Inc, New York, USA) 1993, 479-552.
[21] Tibor Kelen, Mechanical Deformation, in Polymer Degradation, (Van Nostrand Reinhold Company, New York, USA) 1983, 157-172.
[22] R. Chatten, D. Vesely, "Environmental stress cracking of polypropylene" in Polypropylene An A-Z Reference Polymer Science and Technology Series 2 Ed. J. Karger-Kocsis (1999) 206-214.(ISBN: 978-94-010-5899-5)
[23] Arnaud Clave, Hanna Yahi, Jean-Claude Hammou, Suzelei Montanari, Pierre Gounon and Henri Clave, "Polypropylene as a reinforcement in pelvic surgery is not inert: comparative analysis of 100 explants" International Urogynecology Journal and Pelvic Floor Dysfunction 21 (2010) 261-270.

when it does not contain adequate levels of antioxidants to protect against this degradation process.[24,25,26,27,28,29,30,31,32,33,34,35,36,37,38]

In 1976, Liebert et al. studied oxidation of polypropylene filaments with and without antioxidants, which were explanted from hamsters.[39] Explanted samples without an antioxidant showed *in vivo* oxidation of polypropylene; which was evident from the carbonyl band in the IR spectra; which resulted in loss of mechanical properties. Thus, the oxidation process may be effectively retarded if adequate levels of antioxidants are used and remain in the fiber while in the body. This study conducted over 40 years ago demonstrates the same effect as seen in Ethicon's own unpublished studies, as discussed in greater detail below. That is, if polypropylene is not adequately protected with antioxidants, it is susceptible to degradation through the oxidation pathway.

In 1986, Jongebloed *et al* used SEM to analyze an Ethicon Prolene suture and other sutures that were explanted from human eyes. The researchers concluded that after just one-year of

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[24] H.J. Oswald, E. Turi, The Deterioration of Polypropylene By Oxidative Degradation, Polymer Engineering and Science, 5 (1965) 152-158.
[25] H.J. Oswald, E. Turi, The Deterioration of Polypropylene By Oxidative Degradation, Polymer Engineering and Science, 5 (1965) 152-158.
[26] Timothy C. Liebert, Richard P. Chartoff, Stanley L. Cosgrove, Robert S. McCuskey, Subcutaneous Implants of Polypropylene Filaments, J. Biomed. Mater. Res., 10 (1976) 939-951.
[27] Williams, Review Biodegradation of surgical polymers, Journal of Materials Science, 17 (1982) 1233-1246
[28] Apple, Mamalis, Brady, Loftfield, Norman and Olson, Biocompatibility of implant materials: A review and scanning electron microscopic study, Am Intra-Ocular Implant Soc, Vol 10 (1984).
[29] Williams and Sheng P. Zhong, Are Free Radicals Involved in Biodegradation of Implanted Polymers?, Adv. Matter, 3 (1991) 623-626.
[30] S.A.M. Ali, S.-P. Zhong, P.J. Doherty and D.F. Williams, Mechanisms of polymer degradation in implantable devices, Biomaterials, 14 (1993) 648-656
[31] Celine Mary, Yves Marois, Martin W. King, Gaetan Laroche, Yvan Douville, Louisette Martin, Robert Guidoin, Comparison of the In Vivo Behaviour of Polyvinylidene Fluoride and Polypropylene Sutures Used in Vascular Surgery, ASAIO Journal, 44 (1998) 199-206.
[32] Costello, S. L. Bachman, B. J. Ramshaw and S. A. Grant, Materials characterization of explanted polypropylene hernia meshes, Journal of Biomedical Materials Research Part B: Applied Biomaterials 83B (2007) 44-49.
[33] Costello, C.R.., Bachman S.L., Grant S.A. and others, Characterization of Heavyweight and Lightweight Polypropylene Prosthetic Mesh Explants From a Single Patient, Surgical Innovation 14 (2007) 168-176.
[34] Matthew J. Cozad, David A. Grant, Sharon L. Bachman, Daniel N. Grant, Bruce J. Ramshaw, Sheila A. Grant, Materials characterization of explanted polypropylene, polyethylene terephthalate, and expanded polytetrafluoroethylene composites: Spectral and thermal analysis, J Biomed Mater Res B Appl Biomater, 94 (2010) 455-462.
[35] Arnaud Clave, Hanna Yahi, Jean-Claude Hammou, Suzelei Montanari, Pierre Gounon and Henri Clave, Polypropylene as a reinforcement in pelvic surgery is not inert: comparative analysis of 100 explants, International Urogynecology Journal and Pelvic Floor Dysfunction 21 (2010) 261-270.
[36] Donald Ostergard, Degradation, infection and heat effects on polypropylene mesh for pelvic implantation: what was known and when it was known, Int Urogynecol J, 22 (2011) 771-774.
[37] C.D. Klink, K. Junge, M. Binnebosel, H. P. Alizai, J. Otto, U. P. Neumann, U. Klinge, Comparison of Long-Term Biocompability of PVDF and PP Meshes, Journal of Investigative Surgery, 24 (2011) 292-299.
[38] Gina Sternschuss, Donald R. Ostergard, Hiren Patel, Post-Implantation Alterations of Polypropylene in the Human, The Journal of Urology, 188 (2012) 27-32.
[39] Timothy C Liebert, Richard P. Chartoff, Stanley L. Cosgrove and Roberts S. McCuskey Journal of Biomedical Materials Research 10 (1976) 939-951.

implantation "[b]oth prolene loops showed severe degradation of the surface layer."[40] The researchers characterize the morphological features on the surface of several explanted fibers and distinguish very well the different features of biological deposits compared to those associated with degraded Prolene polypropylene.

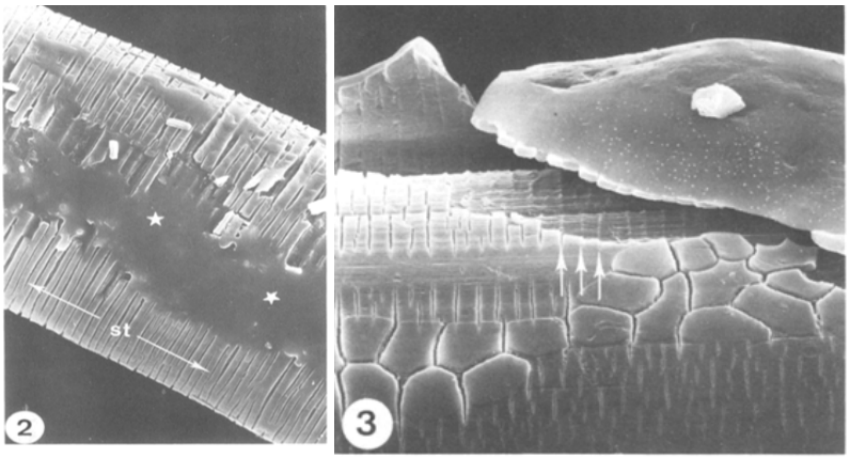

Figure 1- Prolene: Figure 2 (370×), degraded surface; *=deposited organic matter; st=regular pattern of striations. Figure 3 (770×), detail of degraded surface layer. [41]

In 1998, Celine Mary et al. also analyzed Ethicon's Prolene suture in an animal study that compared explanted Prolene[42] sutures received from Ethicon to explanted PVDF sutures.[43]

[40] W.L. Jongebloed, et al, Mechanical and biochemical effects of man-made fibres and metals in the human eye, a SEM-study, Ophthalmologica 61, 303-312 (1986).
[41] Figures adapted from W.L. Jongebloed, et al, Mechanical and biochemical effects of man-made fibres and metals in the human eye, a SEM-study, Ophthalmologica 61, 303-312 (1986).
[42] Prolene is the same polypropylene used by Ethicon in its Prolift, Prosima, TVT and TVT-O products.
[43] Celine Mary, Yves Marois, Martin W. King, Gaetan Laroche, Yvan Douville, Louisette Martin, Robert Guidoin, Comparison of the In Vivo Behaviour of Polyvinylidene Fluoride and Polypropylene Sutures Used in Vascular Surgery, ASAIO Journal, 44 (1998) 199-206.

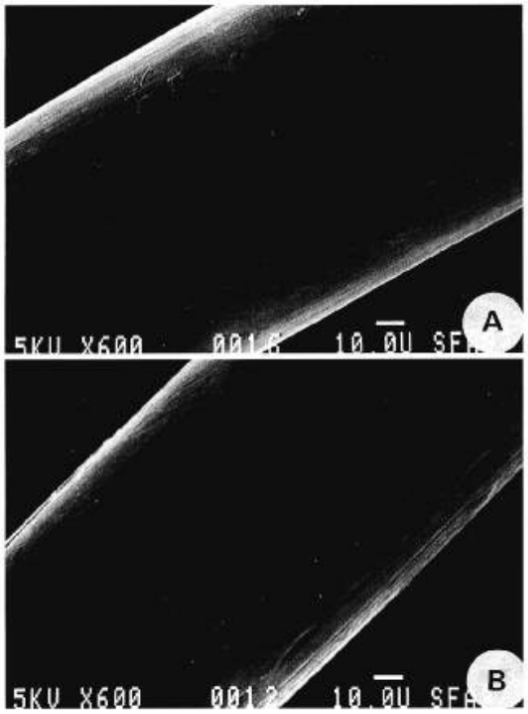

Figure 6. Scanning electron photomicrographs of retrieved and cleaned 6–0 polyvinylidene fluoride sutures showing the surface morphology after implantation for 1 (A, ×600) and 2 (B, ×600) years *in vivo*.

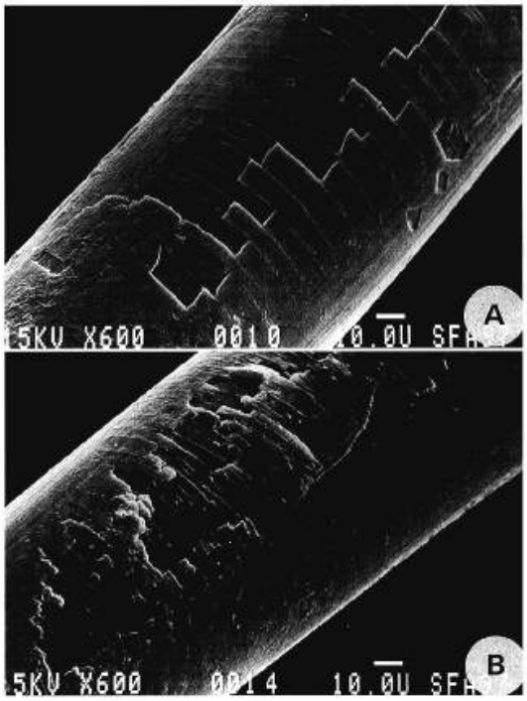

Figure 7. Scanning electron photomicrographs of retrieved and cleaned 6–0 polypropylene sutures showing the surface morphology after implantation for 1 (A, ×100) and 2 (B, ×600) years *in vivo*.

Figure 2- Scanning electron photomicrographs of retrieved and cleaned 6-0 polyvinylidene fluoride sutures showing the surface morphology after implantation for 1 (A, ×600) and 2 (B, ×600) years *in vivo*. Figure 7. Scanning electron photomicrographs of retrieved and cleaned 6-0 polypropylene sutures showing the surface morphology after implantation for 1 (A, ×100) and 2 (B, ×600) years *in vivo*.[44]

As is demonstrated by Dr. Mary and her colleagues in their publication, the surface layer of Prolene degrades in vivo by the enzymatic attack caused by inflammation and the body's immune response to the foreign body while the core remains relatively intact:

> The reason for this stress cracking phenomenon in oriented polypropylene monofilaments has been explained by their pronounced skin/core structure. This bicomponent structure is created by the differential cooling rates between the external and internal layers of the monofilaments during the melt spinning process, which leads to the formation of a low order nonfibrillar outer skin a few microns thick, and a highly oriented crystaline fibrillar inner core. Blais *et al.*. identified a distinct separation and different properties between these two layers. They found that the outer skin is more susceptible to oxidative degradation than the fibrillar inner core. Cleavage of the polymer chains causes relaxation of the folded lamellae, increases in crystallinity and density, and contraction localized to the outer skin. This in turn leads to regular circumferential crack formation at the surface, but only to the depth of the outer layer. Because this cracking is confined to

[44] Figures adapted from Celine Mary, Yves Marois, Martin W. King, Gaetan Laroche, Yvan Douville, Louisette Martin, Robert Guidoin, Comparison of the In Vivo Behaviour of Polyvinylidene Fluoride and Polypropylene Sutures Used in Vascular Surgery, ASAIO Journal, 44 (1998) 199-206.

> the outer skin, which is clearly distinguishable from the inner core structure, it is not surprising to observe that, during abrasive stresses, such as cleaning, there was a tendency for the cracked rings at the surface to flake off and separate from the underlying core material.[1]

As Dr. Mary and her colleagues reported, "it is not surprising to observe that, during abrasive stress, **such as cleaning**, there was a tendency for the cracked rings at the surface to flake off and separate from the underlying core material."[45] Ethicon's experts have previously argued that the cracked surface layer is of biologic origin and that after excessive cleaning of the explants, the FTIR data does not demonstrate strong carbonyl absorbance indicative of oxidized polypropylene. However, Ethicon's experts use oxidizing agents and apply significant abrasive stress over a prolonged period of time to the explanted material which, in my opinion and consistent with those of Dr. Mary and her colleagues, causes the degraded surface layer to flake off leaving a more intact core which is then tested by Ethicon's experts using FTIR or other techniques. The excessive cleaning process that Ethicon's experts use is unreliable and the methods employed by them in testing the material are unreliable in the manner in which those techniques are used by Ethicon's experts.

Dr. Mary, like many other researchers, demonstrated in their study that:

> After 1 and 2 years of implantation the surface of the retrieved and cleaned PVDF sutures did not appear to be substantially modified (fig 6). In contrast, the **polypropylene sutures explanted 1 and 2 years postoperatively showed evidence of surface deterioration, characterized by uniformly spaced circumferential cracking and peeling and flaking of the polymer material in the outermost surface layer** (fig. 7) (emphasis added)

It was concluded that Prolene degrades *in vivo* and, further, that PVDF may have "superior biostability to polypropylene over the long term."

Other scientists have published similar results. In 2007 and in 2010, Costello *et al*. published their results which concluded that polypropylene mesh degrades *in vivo*.[46] Likewise, in 2010, Clave *et al*. published their data from their analysis of 100 vaginal mesh implants that were explanted due to complications. Like the scientists before them, Clave *et al*. found that all polypropylene vaginal mesh devices degrade while *in vivo*.[47]

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[1] Mary, et al., Comparison of the In Vivo Behavior of Polyvinylidene Fluoride and Polypropylene Sutures Used in Vascular Surgery, *ASAIO Journal*, (1998) 44(3):199–206 at p. 205 (emphasis added).

[45] Id.

[46] C.R. Costello, et al., Characterization of Heavyweight and Lightweight Polypropylene Prosthetic Mesh Explants From a Single Patient, Surgical Innovation 14 (2007) 168-176; C. R. Costello, Materials characterization of explanted polypropylene hernia meshes, Journal of Biomedical Materials Research Part B: Applied Biomaterials 83B (2007) 44-49.

[47] Arnaud Clave, Hanna Yahi, Jean-Claude Hammou, Suzelei Montanari, Pierre Gounon and Henri Clave, Polypropylene as a reinforcement in pelvic surgery is not inert: comparative analysis of 100 explants, International Urogynecology Journal and Pelvic Floor Dysfunction 21 (2010) 261-270.

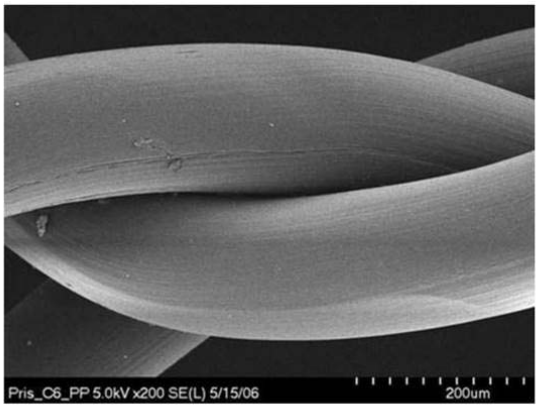


Figure 5. Scanning electron micrograph of heavyweight polypropylene from a pristine Composix E/X mesh.

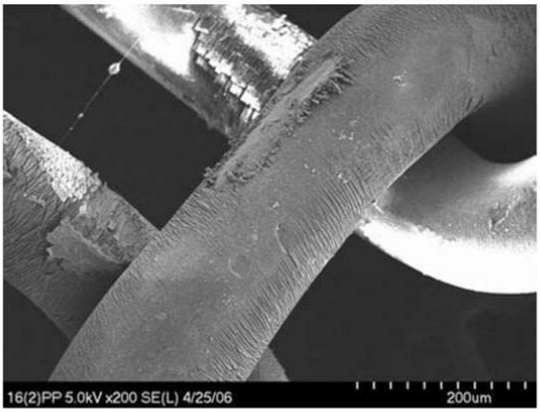
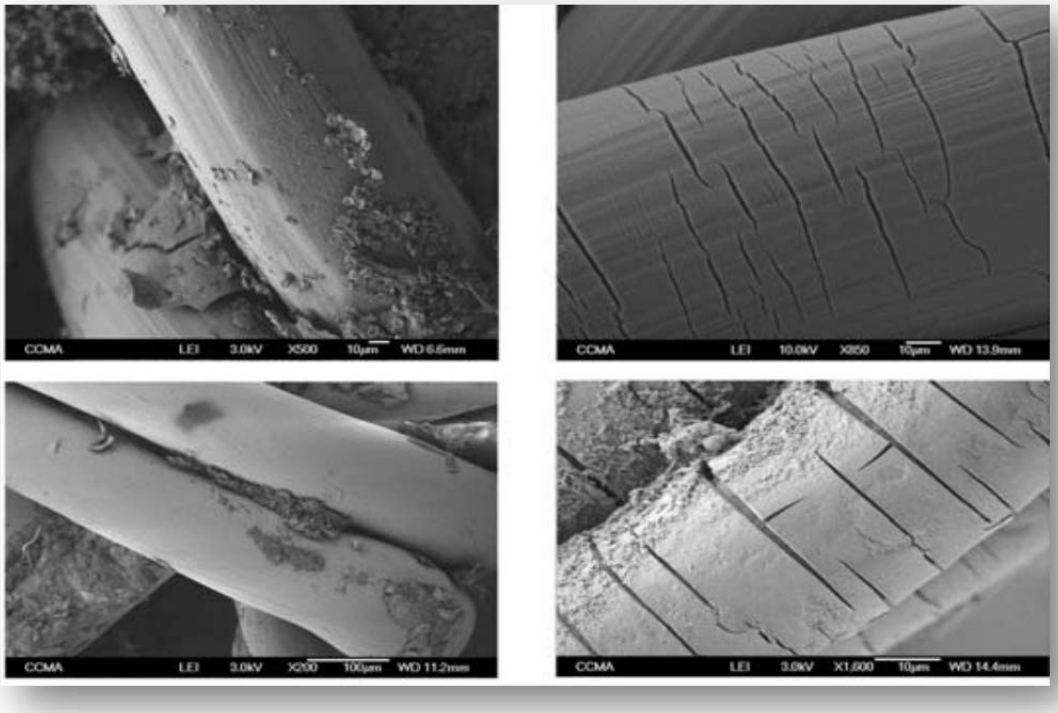


Figure 6. Scanning electron micrograph of heavyweight polypropylene from an explanted Kugel Composix mesh (specimen 2, which remained in vivo for an additional 5 months compared with specimen 1).

Figure 3- Scanning electron micrograph of heavy weight polypropylene from a pristine Composix E/X mesh. Figure 6. Scanning electron micrograph of heavy weight polypropylene from an explanted Kugel Composix mesh (specimen 2, which remained in vivo for an additional 5 months compared with specimen 1). [48]



[48] Figures adapted from C.R. Costello, et al., Characterization of Heavyweight and Lightweight Polypropylene Prosthetic Mesh Explants From a Single Patient, Surgical Innovation 14 (2007) 168-176.

Figure 4- SEM comparison between intact and degraded explants.[49]

In 2013, Wood *et al*.[50] published their data from their analysis of an explanted polypropylene mesh device. Using Scanning Electron Microscopy, these scientists found that the explanted polypropylene mesh fibers (d below) were cracked while the pristine, unused polypropylene fibers of the same product (a below) were smooth:

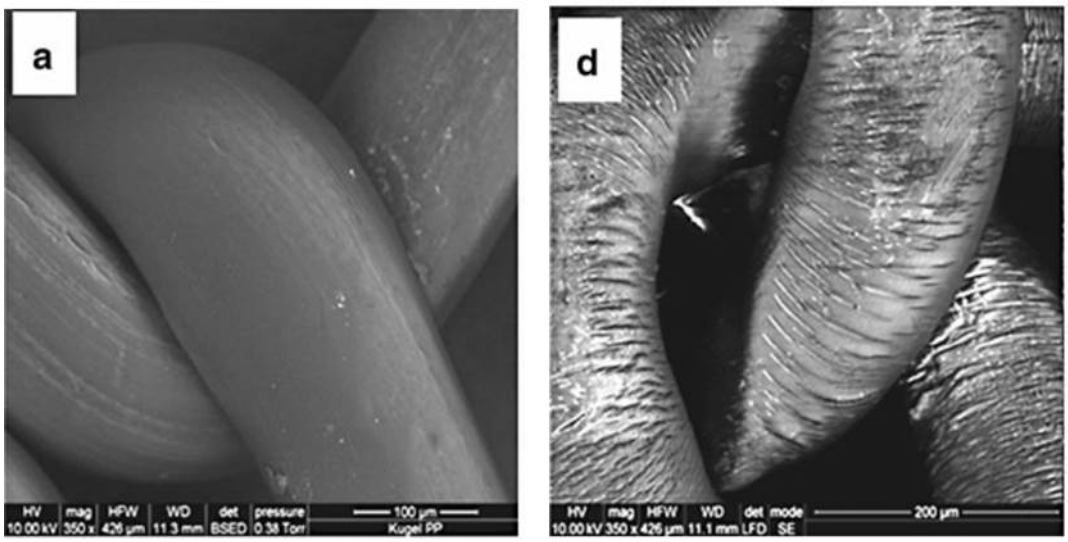


Figure 5- SEM images of pristine (a) polypropylene hernia mesh as well as explanted (d) polypropylene hernia mesh.[51]

To determine why the polypropylene had cracked, these scientists used FTIR. Wood *et al*. concluded that the cracked surface of the explanted polypropylene mesh was caused by oxidative degradation as confirmed by the presence of a carbonyl band at ~1740 cm^{-1}:

[49] Figures adapted from Arnaud Clave, Hanna Yahi, Jean-Claude Hammou, Suzelei Montanari, Pierre Gounon and Henri Clave, Polypropylene as a reinforcement in pelvic surgery is not inert: comparative analysis of 100 explants, International Urogynecology Journal and Pelvic Floor Dysfunction 21 (2010) 261-270.

[50] A.J. Wood et al., Materials characterization and histological analysis of explanted polypropylene, PTFE, and PET hernia meshes from an individual patient, J. Mater Sci: Mater Med (2013) 24:1113-1122

[51] Figures adapted from A.J. Wood et al., Materials characterization and histological analysis of explanted polypropylene, PTFE, and PET hernia meshes from an individual patient, J. Mater Sci: Mater Med (2013) 24:1113-1122

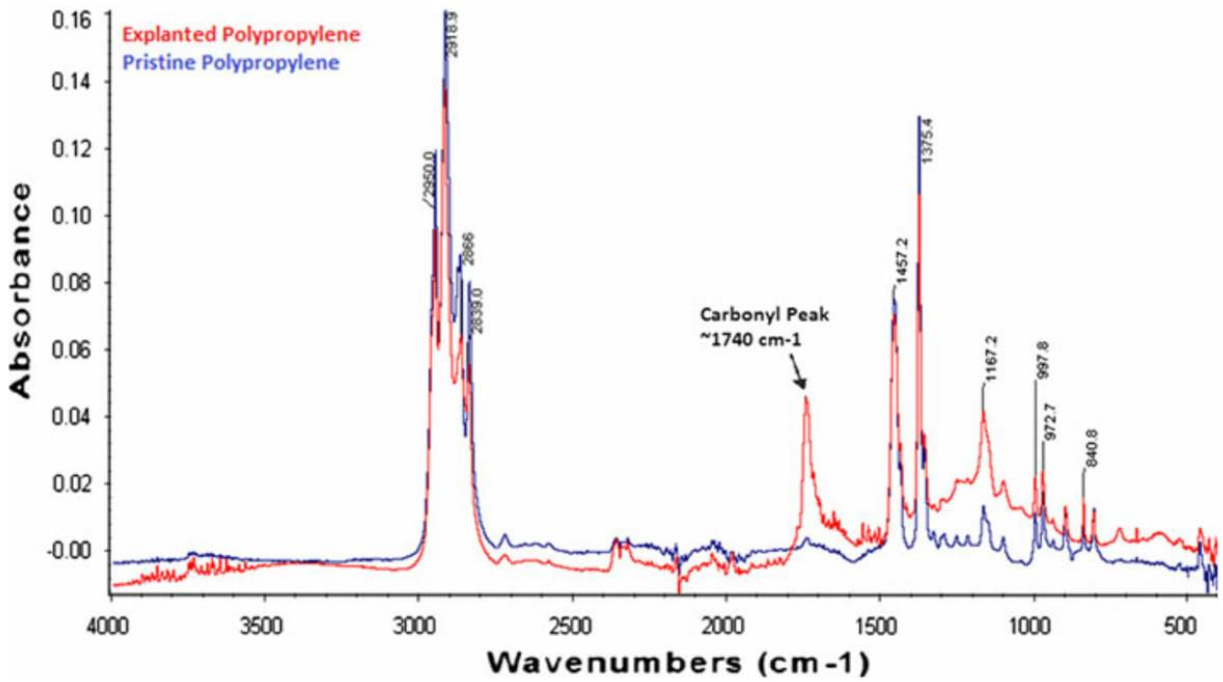


Figure 6- ATR-FTIR scans of pristine polypropylene and a representative polypropylene explant illustrating the carbonyl (C=O) peak.[52]

Similar to the FTIR findings in the Wood article, I have also found evidence that the Prolene in the TVT devices oxidizes which is the likely cause of the degradation and cracking observed on explanted TVT devices:

[52] Figures adapted from A.J. Wood et al., Materials characterization and histological analysis of explanted polypropylene, PTFE, and PET hernia meshes from an individual patient, J. Mater Sci: Mater Med (2013) 24:1113-1122

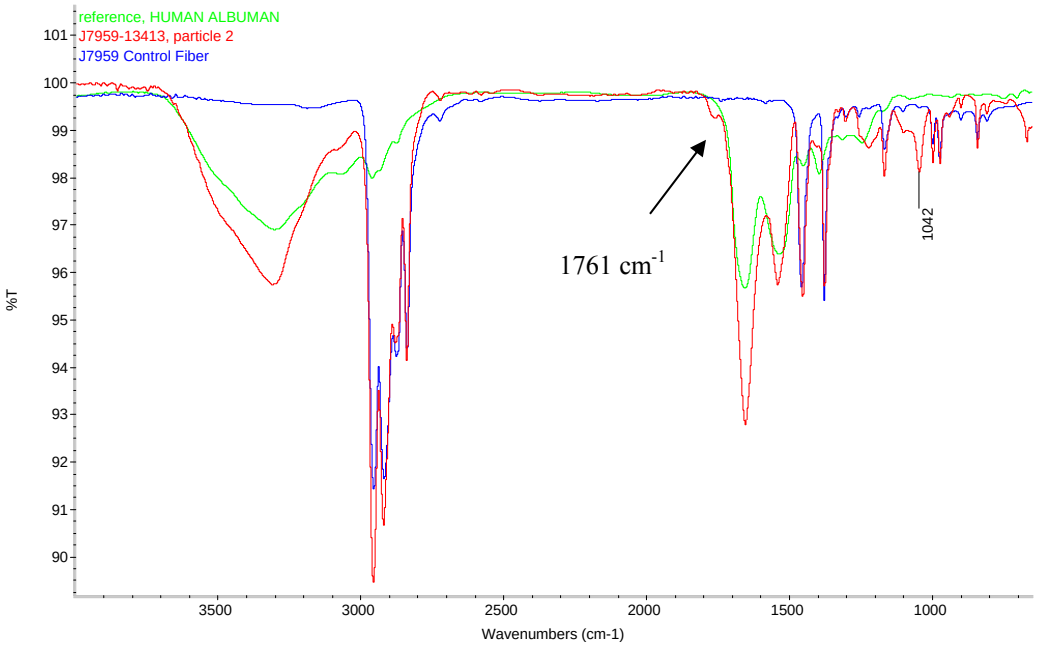


Figure 7- Overlay of FTIR spectra observed by me for explant sample 13413 particle 2 (red), human albumin (green) and control fiber lot 3422128 (blue).

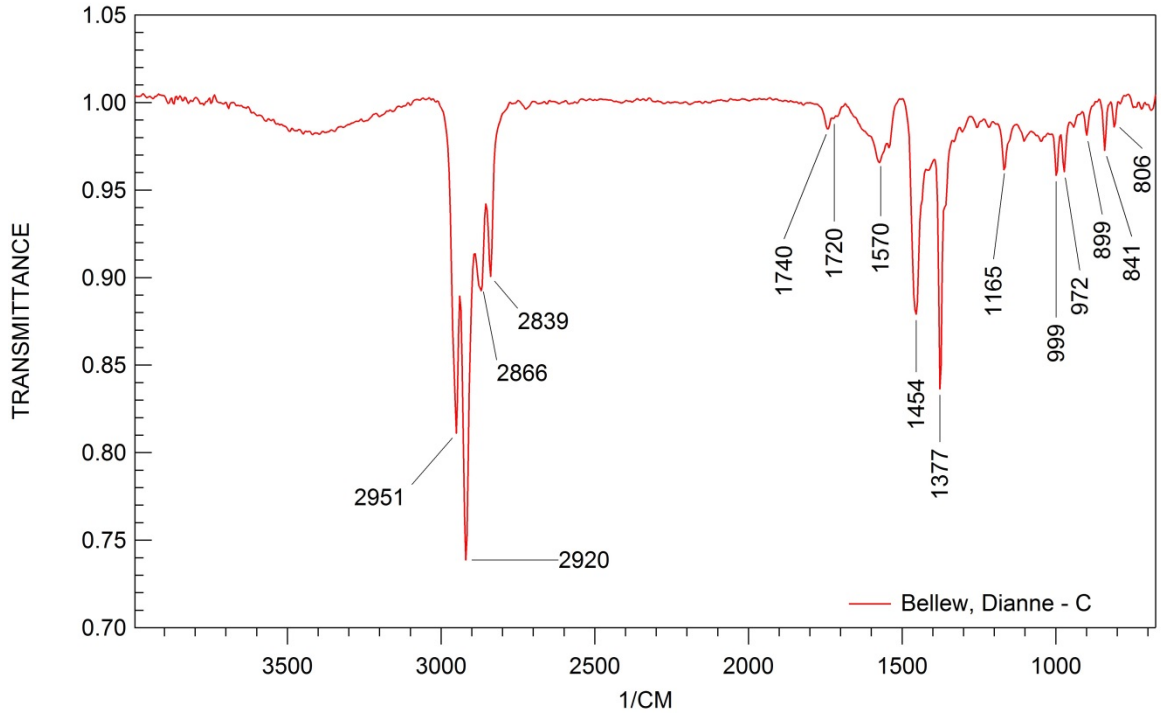


Figure 8: FTIR spectrum from an explanted Ethicon Prolift device which is also manufactured using Ethicon's Prolene polypropylene material – the same Prolene material used in Ethicon's Prosima and TVT devices (sample 35615 - C).

Thus, for more than 50 years scientists who have studied polypropylene degradation have all reached the same conclusion: that polypropylene can degrade through the oxidation and/or environmental stress cracking pathways in the human body. Based on my knowledge, training and experience, my review of the scientific literature, and my review of Ethicon's own internal documents discussed below, it is my opinion to a reasonable degree of scientific certainty that polypropylene, including Ethicon's Prolene mesh device will degrade while implanted in the human body.

IV. Ethicon's Internal Documents Demonstrate that the Prolene Used in Ethicon's Products Undergoes *in vivo* Degradation

My review of Ethicon's internal documents provides additional support for my opinions and findings herein. Ethicon has conducted a number of studies confirming that Prolene degrades *in vivo*.

In 1985, Ethicon started a 10-year dog study that looked at the *in vivo* stability of various polymeric sutures, including Prolene and PVDF. The scientists internally published data from the 10-year dog study at the 2 year, 5 year, 6 year 10.5 months, and 7 year intervals. The data from the 10 year interval was not published because the dogs died prematurely.

On August 10, 1990, Ethicon scientists issued an internal report of their 5-year data from the 10-year dog study.[53] In that report, Ethicon's scientists concluded that "After 5 years *in* vivo the PVDF 5-0 suture was the only explanted material from five dogs which did not show any surface damage due to degradation. Out of seven PROLENE explants, two revealed cracking....The PROLENE surface, intact at the two year point, showed signs of degradation at five years."

The cracking observed on polypropylene is not a formaldehyde protein polymer, as has been previously argued by Ethicon's experts, as formalin was not used in Ethicon's dog study yet cracking was still observed. Moreover, Ethicon's scientists ruled out sample preparation as the cause for the cracking: "It can be said unequivocally that the cracking that was seen in any of the sutures was not introduced by sample preparation, i.e., drying. If cracking was observed on a dry suture in the light microscope or in the SEM, the same cracking was also found on the same suture after it had been in body fluids and then in sterile water, without ever having dried."

On May 29, 1992, Ethicon's scientists issued an internal report of the 10-year dog study after 6 years and 10 months.[54] Ethicon's scientists concluded that "[t]he only explanted suture still undamaged after 6 years and 10.5 months in vivo is the 5-0 PVDF suture" while "[a]ppoximately 50% of the PROLENE suture surface was cracked due to degradation."

On October 15, 1992, Ethicon's scientists issued an internal report of their 7-year data from the 10-year dog study.[55] Ethicon's scientist reported that "IR spectra of the cracked PROLENE specimens (Figure A) showed possible evidence of slight oxidation (a broadened weak

[53] ETH.MESH.11336474
[54] ETH.MESH.09888100
[55] ETH.MESH.09888187

absorbance at about 1650 cm^{-1}) and concluded "[d]egradation in PROLENE is still increasing and PVDF, even though a few cracks were found, is still by far the most surface resistant in-house made suture in terms of cracking."

The 1650 cm^{-1} and 1540 cm^{-1} bands are typically indicative of what are known as the amide-I and amide-II bands respectively of the polyamides.[56] Since proteins are polyamides, they should contain BOTH bands.

It is my opinion to a reasonable degree of scientific certainty that polypropylene mesh placed in the pelvic region of a woman's body will undergo greater degradation than polypropylene placed in the heart of a dog. Numerous studies in the scientific literature discuss the highly-septic, bacteria laden environment of the pelvis and specifically, the vagina.[57] Moreover, the higher surface area in Ethicon's Prolene polypropylene devices leads to greater foreign body reaction, greater inflammatory response and thus, higher amounts of inflammatory mediators attacking the surface of the fibers leading to greater amounts of degradation and oxidation.

While data in the 7 year dog study showed little to no macro molecular weight (Mw) loss, this is not evidence that the Prolene does not degrade. This is likely due to the solubilization of the total sample when only the surface polymer (as shown by SEM images) was in fact degraded. This behavior demonstrates that degradation starts on the surface and is not necessarily a bulk phenomenon. This would be expected as macrophages attack the exposed surface of the polypropylene material.[58] Therefore, even if no gross Mw degradation was observed, it cannot be stated to a reasonable degree of scientific certainty that the polypropylene suture did not degrade.

In fact, in my own experience analyzing explanted polypropylene devices manufactured by Ethicon using Nanothermal analysis, it was clearly shown that there was a vast difference between the melt temperatures at the surface of the explanted Prolene device (121-127 ^{o}C) compared to that of the exemplar (176 ^{o}C). It is known in the literature that the melt point of a polymer decreases with decreasing molecular weight.[59] It was shown using AFM that the depth of the surface cracking was ~ 1 um. In other words, the dissolution of non-cracked

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[56] The Infrared Spectra Atlas of Monomers and Polymers, Sadtler Research Laborataories, Philadelphia, PA 1983, page 471.

[57] Shah, K., Nikolavsky D., Flynn, B. Bacterialogical Analysis of Explanted Transvaginal Meshes, Infections/Inflammation of the Genitourinary Tract: Kidney & Bladder (II); 2013. http://www.aua2013.org/abstracts/archive/abstracts_MP42.cfm; Boulanger L, Boukerrou M, Rubod C, Collinet P, Fruchard A, Courcol RJ, Cosson M. Bacteriological analysis of meshes removed for complications after surgical management of urinary incontinence or pelvic organ prolapse. Int Urogynecol J Pelvic Floor Dysfunct. 2008 Jun;19(6):827-31; A. Vollebregt, A. Troelstra, and C. H. van der Vaart, Bacterial colonisation of collagen-coated polypropylene vaginal mesh: are additional intraoperative sterility procedures useful?, International urogynecology journal and pelvic floor dysfunction, vol. 20, no. 11, pp. 1345–51, Nov. 2009; Berrocal J., Clave H., Cosson M., Debodinance Ph., Garbin O., Jacquetin B., Rosenthal C., Salet-Lizee D., Villet R., Conceptual advances in the surgical management of genital prolapse The TVM Technique; J GynecolObestet Biol Reprod (2004) 33, 577-587; Choi, J et al., Use of Mesh During Ventral Hernia Repair in Clean-Contaminated and Contaminated Cases, Annals of Surgery (2012) 255:1

[58] S. A. M. Ali, S. -P. Zhong, P. J. Doherty and D. F. WIlliams, Biomaterials 14 (1993) 648-656.

[59] G. Natta, I. Pasquon, A. Zambelli and G. Gatti "Dependence of the melting point of isotactic polypropylenes on their molecular weight and degree of stereospecificity of different catalytic systems" Macromol. Chem. Phys.70 (1964) 191-205.

polypropylene during the GPC analysis would render the cracked polypropylene portion insignificant in terms of relative quantities.

Based on my review of the scientific literature, my review of Ethicon's internal documents, including the data from the 7 year dog study and my knowledge, training and experience as a polymer scientist, it is my opinion to a reasonable degree of scientific certainty that the cracked surface of Ethicon's Prolene suture in the 7-year dog study was indeed due to degradation and oxidation. Of note, Ethicon's SEM images of the dog suture showed similar degradation and cracking reported in the scientific publications and is consistent with the degradation and cracking I have observed in my own experience analyzing degraded polypropylene, including the Prolene TVT and Prolift devices manufactured by Ethicon. [See images below] [60]

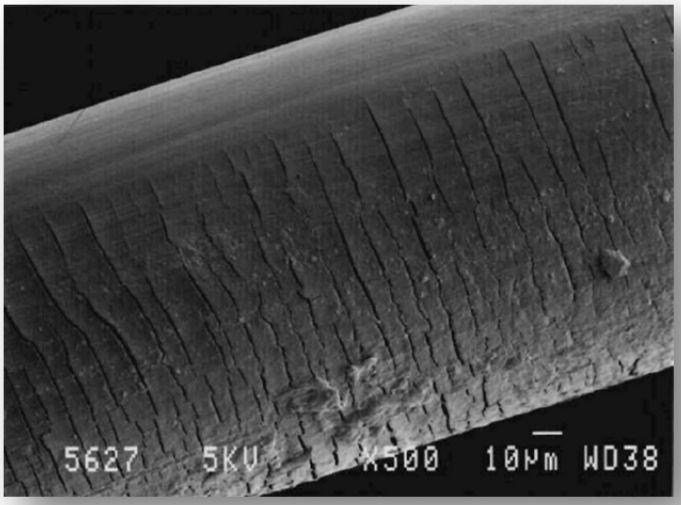

Figure 9- SEM image of suture explanted from a dog by Ethicon.

[60] ETH.MESH.09557798 – Seven Year Dog Study images

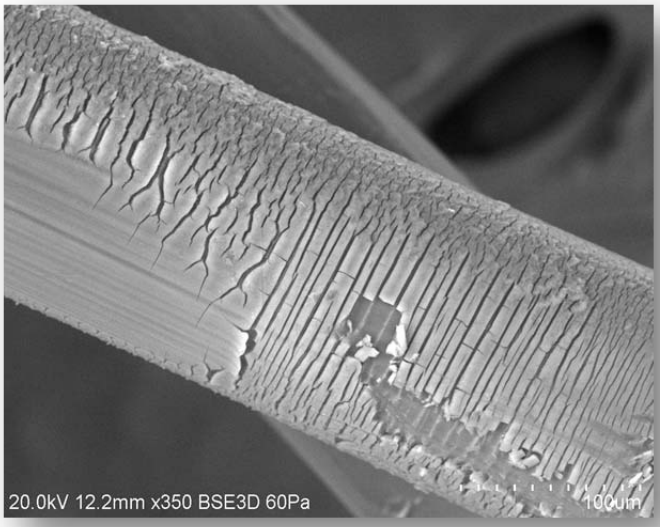

Figure 10- SEM image of explanted TVT device (Sample J7959 A13418)

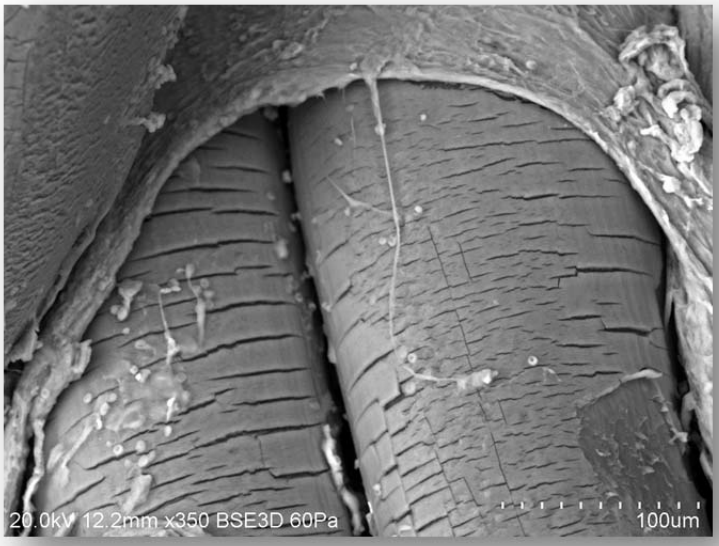

Figure 11- SEM image of explanted TVT device (Sample J7959 13405)

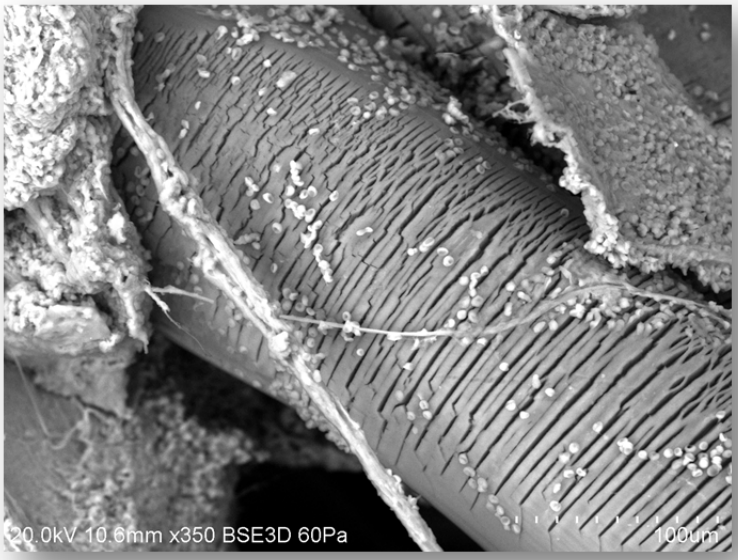

Figure 12- SEM image of explanted TVT device (Sample J7959 13407)

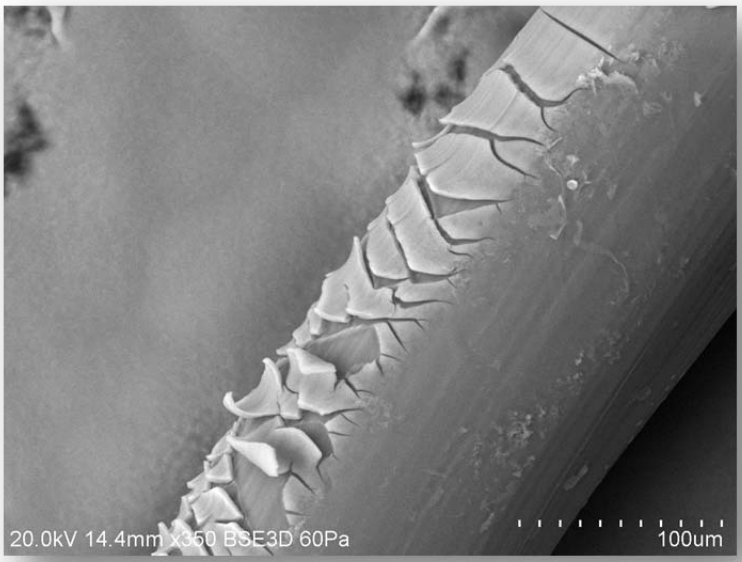

Figure 13- SEM image of explanted TVT device (Sample J7959 13403)

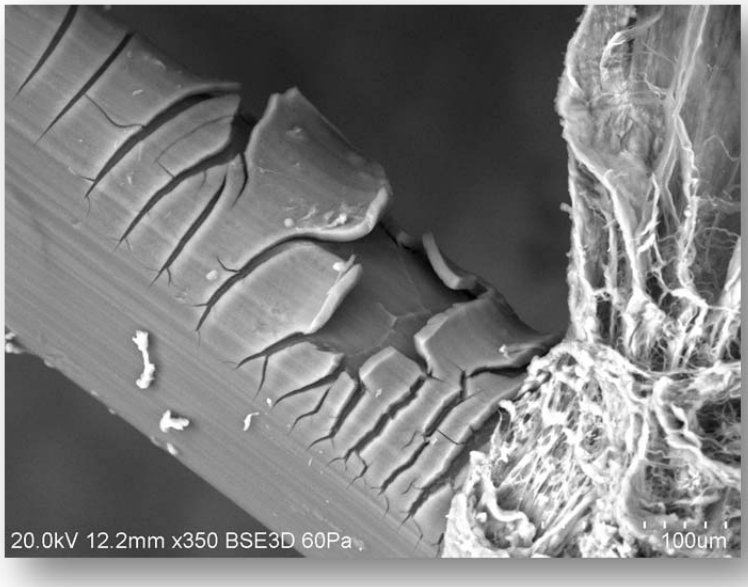

Figure 14- SEM image of explanted TVT device (Sample J7959 13409)

My review of Ethicon's documents also shows that in approximately September of 1987, Ethicon received 58 human Prolene explants that were provided to Ethicon by Prof. Robert Guidoin. On or about January 20, 1988, Ethicon's scientists, using Scanning Electron Microscopy, found that 32 of the 58 Prolene explants were cracked.[61] In an attempt to determine the cause of the cracking observed by SEM on 55% of these Prolene explants, Ethicon's scientists performed melt point and FTIR studies on two, 2 year explants (83D062 and 83TI9020) that had no visual evidence of cracking, on an 8 year explant (83D035) that had visual evidence of severe cracking, and on an unused pristine control.[62] Following these studies, Ethicon's scientist, Daniel Burkley, concluded that:

1. The amount of DLTDP is reduced in the explanted sutures. No DLTDP is observed in the surface scraped (cracked regions) of 83D035. The observed DLTDP decreases with implant time.

2. No protein is observed in any spectra of the explanted sutures.

3. The surface scraped material from the cracked regions 83DO35 has a melting range indicative of degraded polypropylene. The IR spectra of this scraped material is clearly polypropylene, but it appears to be degraded in an oxidative fashion. There are a number of degradation species possible from the IR data. Hydroxyl and acid/ester functionality are definitely present. Ketone and/or unsaturated species are suggested, but not verified.

[61] DEPO.ETH.MESH.00004755
[62] ETH.MESH.13334286

4. The degraded portion of the 8-year explant makes up only a minor portion of the entire suture.

In other words, Ethicon's scientists found that the antioxidant DLTDP, which was supposed to protect the Prolene polypropylene from oxidative degradation, leaches out over time into the surrounding tissue. When this happens, it leaves the Prolene susceptible to oxidation, which causes the Prolene to degrade and crack while implanted in the body.

Ethicon's findings above are consistent with my own experience using melt point methods to analyze explanted Ethicon Prolene mesh devices. I have observed lower melt points using Nanothermal analysis which demonstrated that the explanted device degraded as a result of oxidation, which most likely occurred as a result of *in vivo* leaching of the antioxidants which leaves the Prolene fibers unprotected against oxidation.

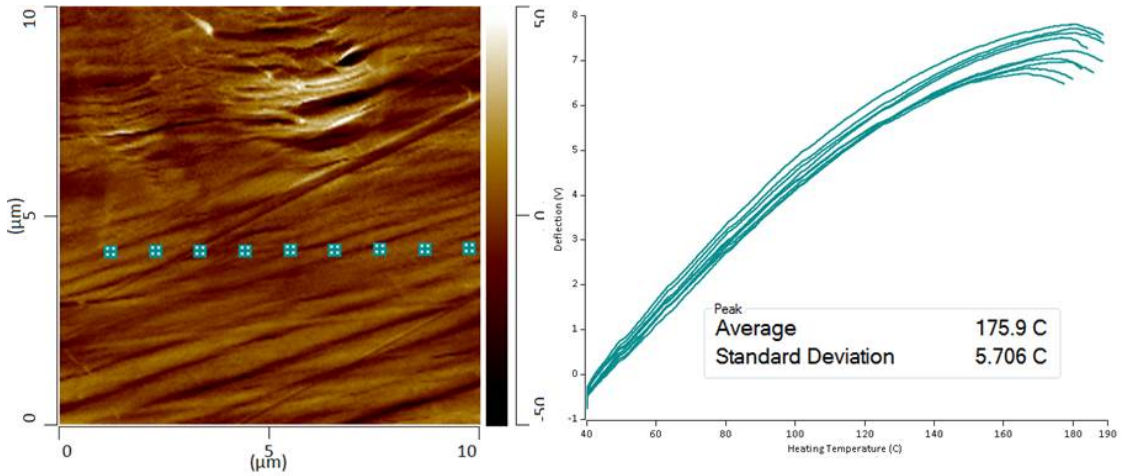

Figure 15 - AFM height image of sample surface of Exemplar A (left). nanoTA measurements obtained from surface of Exemplar A (right).

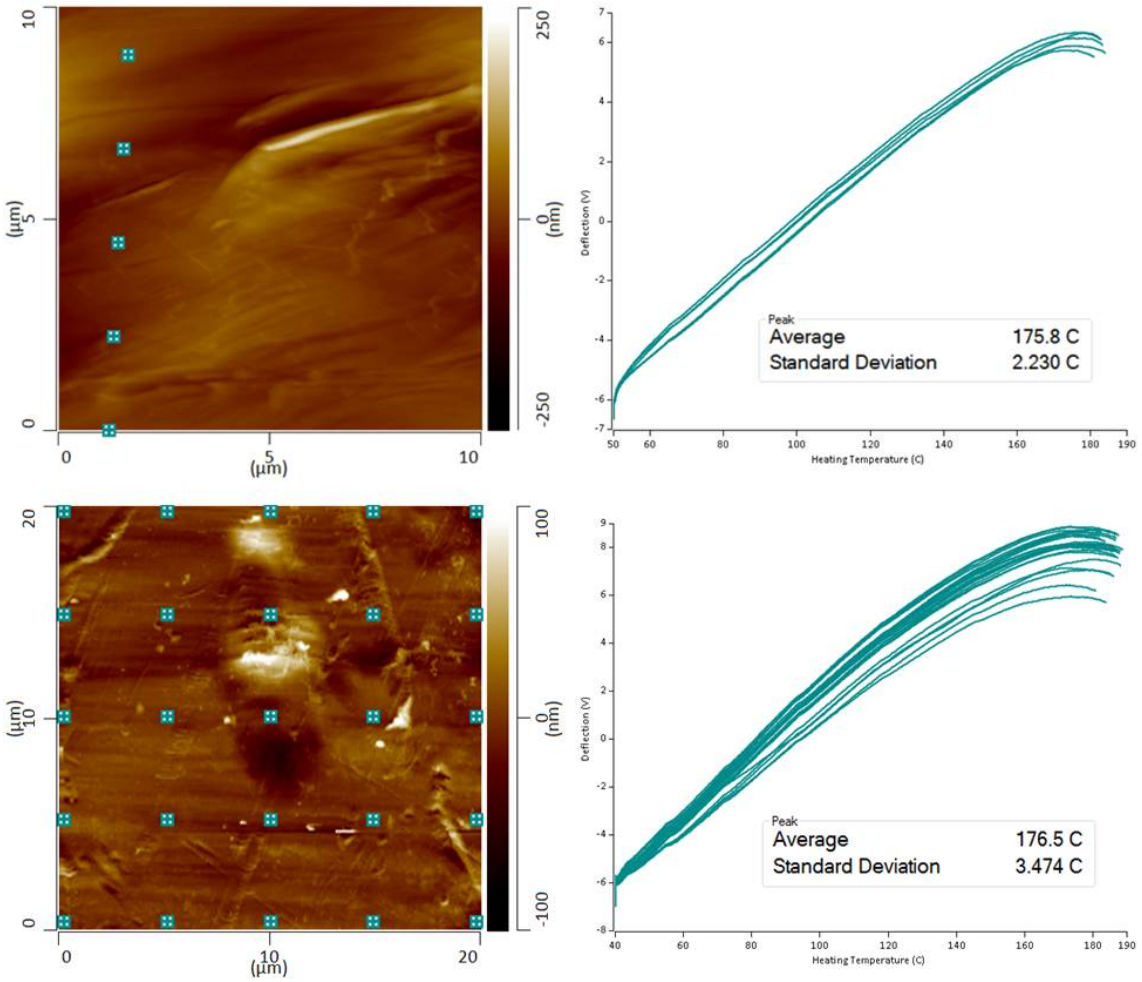

Figure 16 - AFM imaging of Exemplar C (markers on image indicate regions for subsequent nanoTA measurements (left). nanoTA measurements obtained on the surface of Exemplar C (right).

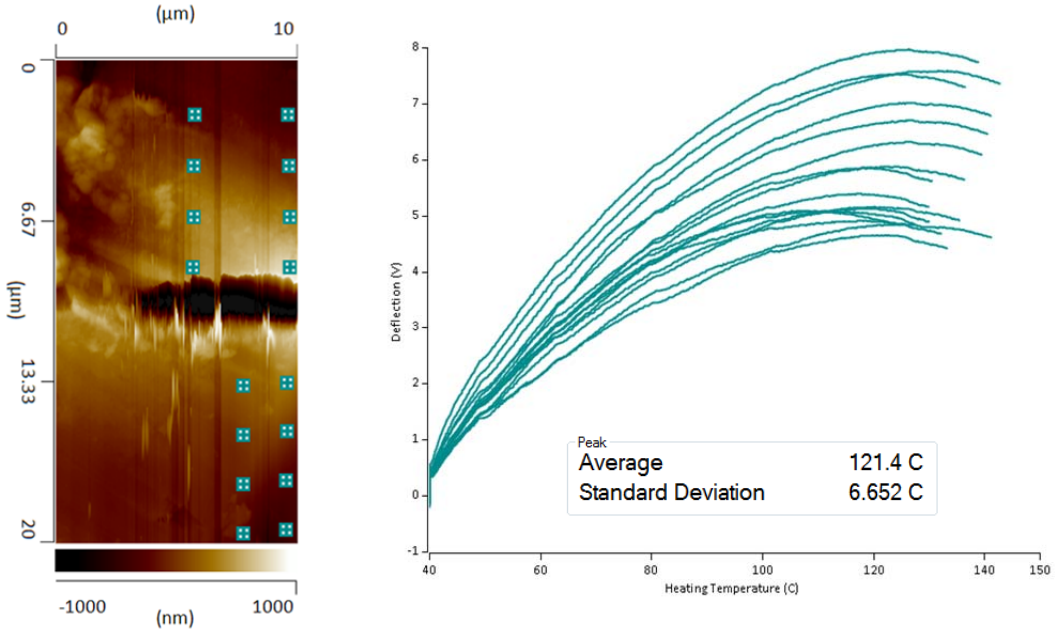

Figure 17 - AFM image of cracked region on Bellew, Dianne B (left). nanoTA measurements obtained around cracked regions on Bellew, Dianne B (right).

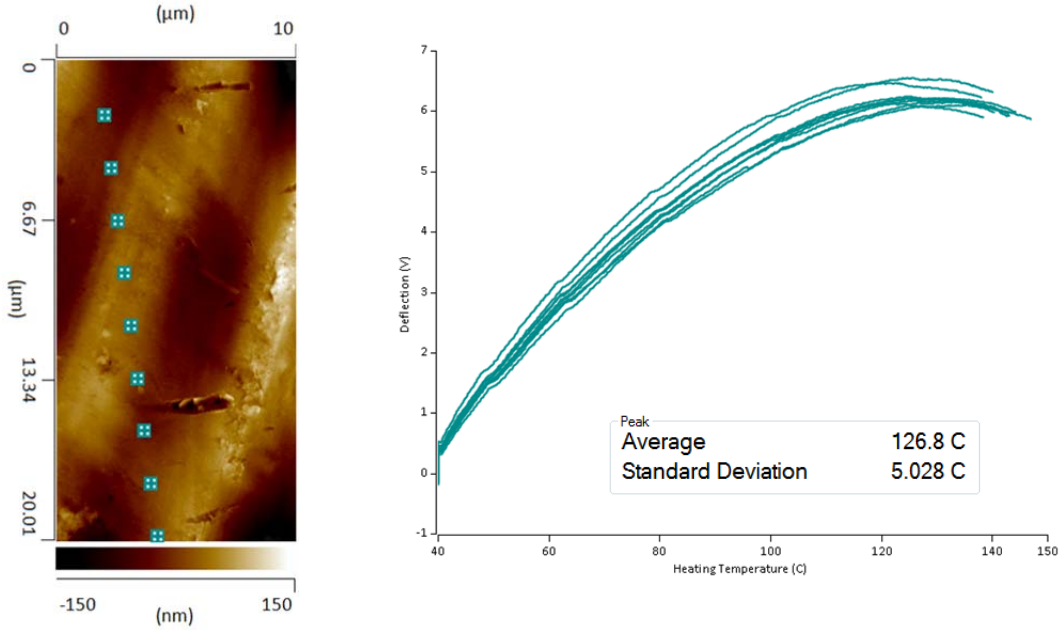

Figure 18 - AFM height image showing surface topography of Bellew, Dianne B fibers in region away from cracks (left). nanoTA measurements obtained away from the cracked regions on Bellew, Dianne B fibers (right).

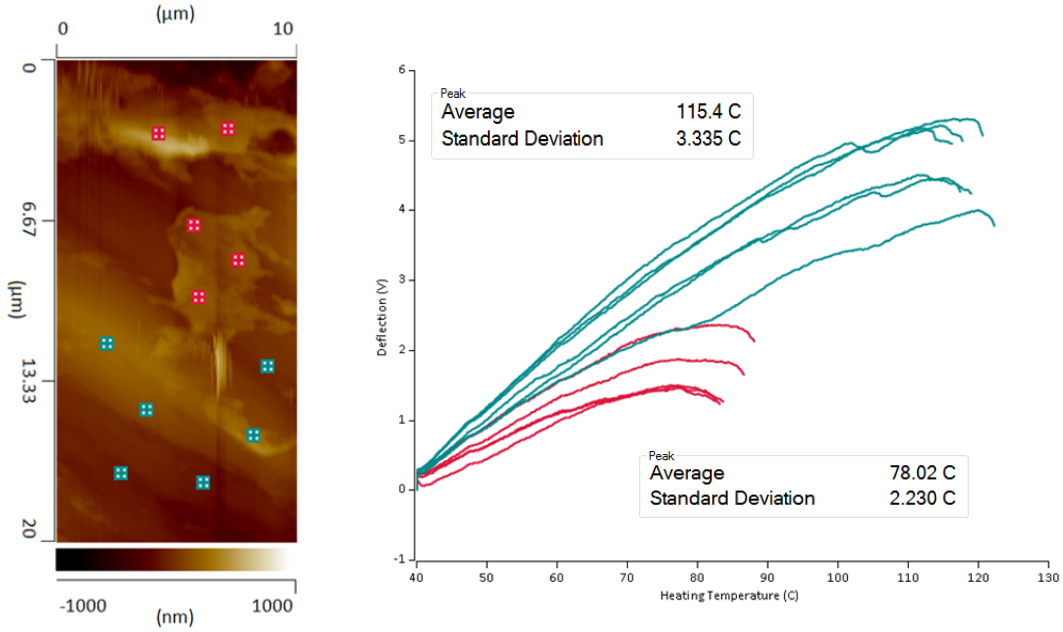

Figure 19 - AFM height image of surface of hypochlorite treated Bellew, Dianne C (left). nanoTA measurements on Bellew, Dianne C both on (red) and off (blue) the flake-like material (right).

Dr. Thomas Barbolt, one of Ethicon's former scientists, testified that the antioxidants leach out of the Prolene mesh fibers into the surrounding tissue[63] making the mesh susceptible to *in vivo* surface degradation.[64] When I have analyzed cracked and degraded TVT devices in my own lab, my findings confirmed Dr. Barbolt's testimony that the antioxidants do leach out of the Prolene fibers leaving the TVT device susceptible to degradation.

As the Mary publication and Ethicon's dog study discussed above demonstrate, PVDF is less susceptible to degradation than Ethicon's Prolene. Recognizing this, in 2007, Ethicon's scientist, Dieter Engel, wrote in an email to his colleagues titled "How inert is polypropylene" explaining that Ethicon would change the material from Prolene mesh to Pronova mesh, a PVDF co-polymer:

> What is the future? We will change the material of our mesh and move to Pronova as the future material platform for mesh, starting with NG TSM. Pronova has a reduced foreign body reaction compared to Prolene, as shown in several animal studies, and will improve the perceived biocompatibility of our mesh. Besides, Pronova is much less susceptible to mechanical damage (as it is less stretched and a different chemical composition); it is much easier to process in the knitting machines, less quality issues.[65]

Ethicon's own studies and testimony from Ethicon's scientists confirm the same findings from scientists throughout the scientific community: that polypropylene – and specifically Prolene – is

[63] Deposition of Dr. Thomas A. Barbolt (1/8/14) at 360:20-361:6
[64] Deposition of Dr. Thomas A. Barbolt (1/8/14) at 408:13-409:13
[65] ETH.MESH.05588123

subject to *in vivo* degradation. In fact, based on my review of the published scientific literature and Ethicon's internal documents, a vast majority of scientists who have studied polypropylene for degradation have consistently concluded that polypropylene (including Prolene) undergoes *in vivo* degradation. Moreover, both internal and external scientists have concluded that PVDF is a more stable polymer than Prolene as a long term, permanent implant.

Therefore, based on my knowledge, training and experience, my review of the scientific literature and my review of the internal Ethicon documents, it is my opinion to a reasonable degree of scientific certainty that, over time, the antioxidants contained in Prolene leach out of the fibers, in to the surrounding tissue, which leads to oxidation, *in vivo* degradation and cracking.

It is further my opinion to a reasonable degree of scientific certainty that PVDF/PVDF co-polymers (like Pronova), is a reasonable alternative design, in terms of degradation and long term stability, than Prolene.

Ethicon's own internal studies as well the scientific literature demonstrate that Prolene degrades *in vivo* and that Ethicon had an alternative polymer which was more stable than Prolene in the long term.

Based on my knowledge, training and experience, my thorough review of Ethicon's internal documents and scientific publications, as well as my own data, I intend to offer opinions that (1) polypropylene degrades; (2) that as a result of the chemical and physical degradation that occurs while in the body, Ethicon's Prolene mesh devices become brittle and cracks which can peel off the surface into the surrounding tissue; and (3) that explanted Prolene mesh devices manufactured by Ethicon do undergo *in vivo* surface changes consistent with oxidative degradation or environmental stress cracking. My findings and opinions contained herein and in my prior Rule 26 Expert Reports are consistent with the scientific literature on this subject as well as Ethicon's internal studies.

V. SUMMARY OF OPINIONS:

Based on my knowledge, training and experience, my review of the scientific literature, and my review of Ethicon's internal documents, it is my opinion to a reasonable degree of scientific certainty that:

1) Polypropylene can and does undergo *in vivo* degradation;

2) Prolene used to manufacturer Ethicon's Prolene pelvic floor and stress urinary incontinence devices can and does undergo *in vivo* degradation;

3) The antioxidants used to protect Ethicon's Prolene pelvic floor and stress urinary incontinence devices from oxidation leach out of the mesh fibers into the surrounding tissue leaving the TVT devices highly susceptible to *in vivo* degradation;

4) *In vivo* degradation causes Ethicon's Prolene pelvic floor and stress urinary incontinence devices to become brittle which is demonstrated by significant cracking observed in the peer-review publications and Ethicon's internal documents and which is consistent with my own experience in observing these devices under SEM ;

5) As a result of the manufacturing process, Prolene is susceptible to environmental stress cracking;

6) Cholesterols and fatty acids absorbed into Ethicon's Prolene pelvic floor and stress urinary incontinence devices which make the devices susceptible to environmental stress cracking which likely contributed to the degradation and cracking *in vivo* as observed in the SEM images.

VI. RECENT TESTIMONY (HOWARD JORDI, PhD)

Deposition/trial testimony:

Diversified Biotech, Inc. vs. GA International, CA Provided service work, consultation, pre-trial preparation and appeared in court in April 2007. To the best of my recollection, we believe that the case was settled on that day. This contention is supported by White and Fudala LC.

Howmedica Osteonics Corp. vs. Zimmer, Inc., Centerpulse Orthopedics, Inc., Smith&Nephew, Inc. Deposed (2006). Case settled, never went to trial based on my records.

Unisource Worldwide, Inc. v. Stone Plastics, Inc., Global Manufacturing Packaging Solutions, LLC Deposed 2008, Testified 2008

Gary Lamoureux, World Wide Medical Technologies, LLC, Advanced Care Pharmacy, Inc., Advanced Care Pharmacy, LLC and Advanced Care Medical, Inc. vs. AnazaoHealth Corporation, F/K/A GENESIS PHARMACY SVC., INC., D/B/A CUSTOM CARE PHARMACY Deposed 2008

United States v Dennis Beetham and DB Western Inc., Testified June 2010

Hoffman Angelie

Carolyn Lewis v Ethicon, Testified by Deposition in Oct 2013 and Jan 2014 and Testified at Trial in Feb 2014

Linda Batiste v Ethicon, Testified at Trial in March 2014

Bellew v Ethicon, Testified by Deposition on August 19, 2014.

Wheeler v Bard, Testified by Deposition on November 18, 2014.

VII. COMPENSATION

I am compensated for investigation, study and consultation in this case at the rate of $350.00 per hour.

This 1st day of February, 2016

Howard Jordi, Ph.D.